# Modified vaccinia virus Ankara vector and the multi-variant COVID-19 solution

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**The MVA/S1 is perhaps the best candidate for multi-variant vaccine solution to COVID-19. MVA stands for Modified vaccinia virus Ankara. It is a modified poxvirus that has been engineered as a vaccine against a number of diseases and infections. MVA infection provokes the production of type I interferons in conventional dendritic cells (cDCs), but not in plasmacytoid dendritic cells (pDCs). In Covid-19, the type 1 interferons were found to be reduced in pDCs, while the overall number of cDC subsets in the blood become lower. Dendretic cells are antigen presenting cells that play a role in the stimulation of T-cells and B-cells for immune response. Dendretic cells engulf pieces(antigens) of the virus and present those antigens to the defense components of the immune system. The major components of the immune response are T-cells and B-cells. There are 2 forms of T-cells. Helper T-cells and Killer T-cells. During antigen presentation, Helpter T-cells stimulate B-cells to make antibodies. Killer T cells attack cells that have been infected by a foreign pathogen. cDCs are the antigen-presenting cells that can be activated via Toll-like receptors (TLRs), RIG-I-like receptors, and cytosolic DNA-sensing pathways. pDCs are the type I interferon producing cells that sense viral infections via TLR7, TLR8, and TLR9, and their adaptor MyD88. The triggering of TLR receptors by viral nucleic acids leads to the activation of transcription factor interferon regulatory factor-7 (IRF7). MVA infection of cDCs induces type I interferon production and is dependent on STING(stimulator of interferon genes) and interferon regulatory factor-3 (IRF3). The STING/IRF3 pathway can be activated by secondary messanger cyclic GMP-AMP (cGAMP), which is produced by cyclic GMP-AMP synthase (cGAS) in response to viral DNA or RNA. MVA infection of cDCs would enhance antiviral activity as it relates to antigen presentation.**

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**MVA infection of pDC, however, does not induce type I interferon response. Induction of type 1 interferon in pDC is triggered by pDC's use of complex information from TLR signaling and microenvironmenal factors. The mechanism responsible for this is unknown.**

**The use of the Modified vaccinia virus Ankara(MVA) vector for a COVID-19 vaccine has been in production. Researchers at Emory University, the University of Texas Medical Branch and the Ragon Institute used 2 MVA vaccines with different methodologies. The method of the first vaccine involved the expression of the full length spike protein attached to the cell membrane, but before fusion with the membrane. This is the MVA/S vaccine. The method of the second vaccine is the expression of only the S1 region of the secreted spike protein in its trimeric state. This is MVA/S1 vaccine. S is a large, trimeric glycoprotein that mediates the virus's binding to host cell receptors and fusion of virus and host cell membranes through its S1 and S2 subunits. S1 is responsible for the virus binding to the host cell receptor, while S2 is responsible for fusion of the virus to the host cell membrane. Both of these vaccines contain the receptor binding domain (RBD) which is a target of neutralizing antibodies. The first vaccine (MVA/S) elicited antibodies that binded to the RBD, S1, and S2 proteins. The second vaccine (MVA/S1) induced antibodies against the non RBD unit of the S1 subunit. This means that the second vaccine (MVA/S1) can induce antibodies that are non-RBD specific, a very important key in the multi-variant solution. However, MVA/S was capable of inducing a stronger neutralizing antibody response. However, this response was RBD specific. This implies that the MVA/S vaccine would be effective against the specific SARS-CoV-2 variant, but would have to be modified against new variants. I hypothesize that the type 1 interferon response was induced in conventional dendritic cells (cDCs) in the first vaccine (MVA/S), which thus led to more antigen presentation, which then allowed for more neutralizing antibodies to be produced. While the neutralizing**

**antibody response was less in the second vaccine (MVA/S1), MVA/S1 may have induced the type 1 interferon response in plasmacytoid dendritic cells (pDCs) and initiated early viral clearance by activation of Killer T-cells. This would limit the level of antigen presentation needed for the production of more neutralizing antibodies. Since MVA/S1 is RBD non-specific, it could serve as a multi-variant vaccine solution.**

## Bibliography

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